

REMARKS

Applicants respectfully request reconsideration and allowance of all pending claims.

I. Status of the Claims

Applicants previously cancelled claims 1-33. In this Amendment B, claims 34, 37, 39-41, 46, 48, 51 and 53 have been amended, while claims 35 and 36 have been canceled, in order to more particularly claim certain embodiments of the present invention. Support for these amendments may be found within the claims as previously presented. Additionally, support for the amendment to: claim 34 may be found in claims 35 and 36 (both now cancelled); claim 40 may be found in paragraph [0003] of the published application (i.e., U.S. Patent Application Publication No. 2007/0071672); and, claim 51 may be found in claim 46, as well as on page 13, second row, second structure, of the published application (claim 51 being amended to remove structure 2, as well as the structure which is identical to structure 2 but identified as structure 6, and to insert the correct structure for structure 6, therein).

Accordingly, upon entry of this Amendment B, claims 34 and 37-53 remain pending.

II. Amendment to the Specification

Applicants have requested herein that the Specification be amended consistent with the Office's objection on page 5, paragraph 9, of the present action, in order to insert the heading "Brief Description of the Drawings." Accordingly, Applicants request that this objection be withdrawn.

III. Allowable Subject Matter

Applicants acknowledge that claim 52 has been found to be allowable, if rewritten in independent form to include all of the limitations of the claims from which it depends.

IV. Rejection of Claims under 35 U.S.C. §112, Second Paragraph

The Office has rejected claims 34, 37, 40, 45, 48 and 50 as indefinite under 35 U.S.C. §112, second paragraph. For the reasons set forth in detail below, Applicants request reconsideration of this rejection.¹

¹ It is noted that although the Office specifically references only these claims on page 2, paragraph 4, of the present action, the Office subsequently references and appears to reject claims 34-45, 47-50 and 53 under 35 U.S.C. §112, second paragraph. Accordingly, all of these claims will be discussed here.

A. Claims 34-45 and 47-50

The Office appears to have rejected claims 34-45 and 47-50 as indefinite for use of the phrase "the other one is optionally a monodentate ligand" in claim 34. Respectfully, it appears the Office is misreading the claim. As written, claim 34, from which claims 37-50 depend, provides for two alternative definitions for variables X1, X2 and X3. Specifically, claim 34 states that **at least two** of X1, X2 and X3 are monodentate ligands, **or** two of X1, X3 and X3 are part of a bidentate ligand (for example X1 and X2, or X2 and X3, or X1 and X3) and the other (i.e., X3, or X1, or X2, respectively, of the preceding examples) is a monodentate ligand.

Accordingly, Applicants submit claim 34 is **not** ambiguous. One of ordinary skill in the art would clearly understand the meaning and scope of the claim as pending.

B. Claim 37

The Office has rejected claim 37 for use of the phrase "and organic molecules having one of this group as an integral part." Applicants have amended claim 37 by removing this phrase, thus obviating the rejection.

C. Claims 39 and 40

The Office has rejection claim 40 based on the assertion that "it is unclear what organic groups contain a thioether functional group or a terminal NC group." It is noted that claim 40 does not reference a thioether, but claim 39 does. Accordingly, Applicants assume the Office intended to reject claim 39 here, as well.

As amended, claim 39 no longer includes the phrase "and organic molecules containing a thioether functional group." Applicants submit that this amendment obviates any rejection of claim 39.

As amended, claim 40 states that the isocyanides are selected from the group consisting of "an alkyl chain" comprising a terminal NC group coupled thereto, and optionally comprising one of the other substituents recited therein. Applicants submit that this amendment obviates the rejection of claim 40, as well, given that one of ordinary skill in the art would clearly understand the meaning and scope of this claim.

D. Claim 45

The Office has rejected claim 45 for use of the phrase "with guanine or guanosine being present in a slight excess over rhenium or technetium." The Office is of the opinion that the claim is indefinite as a "slight excess" will vary from person to person. However, claim 45 is directed to a laboratory testing procedure in which an amount of the compound is incubated with a slight molar excess of guanine or guanosine and the amount of guanine or guanosine bound to the metal center is determined. If two of the ligands are exchanged by guanine or guanosine

after the three day incubation period, the starting complex is considered to have utility for cancer treatment (see, for example, paragraph [0021] and Example 3 of the published U.S. application). Accordingly, the "slight excess" recited in claim 45 is a reference to a molar excess used in a testing procedure and is not dependent on the characteristics of patients to whom the compound is administered and claim 45 is definite.

E. Claims 48 and 53

The Office has rejected claims 48 and 53 as indefinite for use of the phrase "derivatives or analogues thereof." Applicants have amended the claims by removing the phrase, thus obviating this rejection.

The Office has also rejected claims 48 and 53 as indefinite for use of the phrase "nucleus targeting molecules such as anthracyclines, acridines and other intercalators." Applicants have amended the claims by removing the phrase "nucleus targeting molecules such as" and the phrase "and other intercalators, and derivatives or analogs thereof". Applicants submit these amendments obviate this rejection, as well.

F. Claim 50

The Office has rejected claim 50 as indefinite for use of the term "prodrug", reasoning that it is not clear what components make up the prodrug. Applicants submit that it is clear that the metal tricarbonyl compound of claim 34 may itself be the prodrug. According to the specification, the compound may act as a prodrug as the bound ligands of the compound may be released from the compound to generate the active form of the drug when the pH increases in cancer cells. In some embodiments, X_2 and X_3 may represent the protecting group ligands(s) which are released in the cell to form the active drug. (See paragraphs [0033] and [0034] of the published U.S. application.) Thus, the specification makes it evident that the ligand itself may be the prodrug, and that the composition of the prodrug is evident to one of ordinary skill in the art.

V. Rejection of Claims under 35 U.S.C. §102

A. Ardizzoia et al.

The Office has rejected pending claim 51 as anticipated by Ardizzoia et al. (European Journal of Inorganic Chemistry, 1998) under 35 U.S.C. §102(b), in view of compound 18 therein. In response thereto, it is to be noted that compound 18 has been deleted from pending claim 51. Applicants submit that none of the other compounds

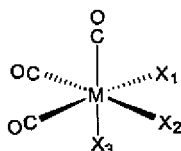
disclosed by Ardizzoia et al. are among the compounds remaining in claim 51. Accordingly, claim 51 is novel over the cited reference.²

B. Smith et al.

The Office has also rejected pending claims 34 and 46-48 as anticipated by Smith et al. ("Radiochemical Investigations of [¹⁸⁸Re(H₂O)(CO)₃-Diaminopropionic acid-SSS-bombesin(7-14)NH₂]: Syntheses, Radiolabeling and *In Vitro/In Vivo* GRP Receptor Targeting Studies") under 35 U.S.C. §102.³ Applicants submit that the pending claims are novel over the disclosure of Smith et al. for the reasons set forth in detail below.

Smith et al. is directed to development of a rhenium radiolabeled bombesin analog that maintains the high binding affinity of bombesin toward GRP receptors. More specifically, Smith et al. developed and tested the radiometallated and the non-radioactive metallated bombesin conjugate, Re(H₂O)(CO)₃-Dpr-(X)-bombesin (7-14)NH₂ (see Scheme 2 on p. 66 for the reaction route to the radiometallated conjugate). The Re(H₂O)(CO)₃-Dpr-(X)-bombesin (7-14)NH₂ conjugate of Smith et al. contains a bidentate ligand, bombesin, bound to rhenium and a monodentate ligand, H₂O.

Pending claim 34, from which claims 46-48 depend, is directed to a method for the treatment of a cancer. The method comprises administering to a patient afflicted with the cancer a metal tricarbonyl compound of the general formula:



wherein: M is rhenium or technetium or an isotope thereof; at least two of X₁, X₂ and X₃ are monodentate ligands **selected from the group consisting of CO, NH₃, aromatic heterocycles, thioethers and isocyanides; or alternatively**, two of X₁, X₂ and X₃ are part of a **bidentate ligand** and the other one of X₁, X₂ and X₃ is a monodentate ligand **selected from the group consisting of CO, aromatic heterocycles, thioethers and isocyanides.**

Accordingly, claim 34 requires that, when two of X₁, X₂ and X₃ of the tricarbonyl compound are part of a bidentate ligand, the other of X₁, X₂ and X₃ is a monodentate ligand selected from the group consisting of CO,

² It is to be noted that claim 51 has also been amended to remove structure 2, as well as the structure which is identical to structure 2 but identified as structure 6, and to insert the correct structure for structure 6, therein.

³ It is noted that the Office cites this reference under 35 U.S.C. §102(b). However, given that this application published the same year as Applicants' earliest priority date, Applicants assume the Office intended to cite this reference under 35 U.S.C. §102(a), and will address the rejection in that context.

aromatic heterocycles, thioethers and isocyanides. Notably, the H₂O monodentate ligand disclosed by Smith et al. is **not** among the monodentate ligands listed by claim 34. Claim 34 is therefore novel over the cited reference, as well as all claims depending therefrom.

CONCLUSION

In view of the foregoing, Applicants respectfully request reconsideration and allowance of all pending claims.

The Commissioner is hereby authorized to charge Deposit Account No. 13-1160 for any fees that may be required for this Amendment B.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Anthony R. Kinney", with a stylized flourish at the end.

Anthony R. Kinney, Reg. No. 44,834
Mallinckrodt Inc.
675 McDonnell Boulevard
Hazelwood, Missouri 63042
(314) 654-3960

VIA EFS